Clinical Chemistry Question and Answer

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Q: What is paraquat poisoning?

A: Introduced in 1962, paraquat is the most important of the bipyridyl family of nonselective herbicides. In a 1977 review by Harley et al., about 600 deaths worldwide were due to accidental or intentional ingestion [1]. The 1994 report of the American Association of Poison control Centres revealed that the accidental exposure appeared to be increasing in the US [2] Recently, there have been some reports of homicidal poisoning by paraquat [3].

Paraquat is available in a liquid concentrate as granules designed to be dissolved in water and used as an aerosol. Paraquat exerts its herbicidal activity by interfering with intracellular electron transfer systems, thereby inhibiting reduction of NADP to NADPH during photosynthesis. This leads to the formation of superoxide, single oxygen, and hydroxyl and peroxide radicals. Their presence cause the destruction of lipid cell membranes by polymerization of unsaturated lipid compounds. Human toxicity is thought to follow a similar mechanism with depletion of the naturally occurring superoxide dismutase. This induces an inflammatory process and irreversible pulmonary fibrosis due to a selective accumulation of paraquat in the lungs.

There are three major routes of paraquat exposure. The most common is accidental or intentional oral ingestion. A solution of paraquat is dark brown colour, and resembles root beer, cola, dark vinegar and soy source. Since the paraquat solution is tasteless, it can be easily used for homicide attempts. The second most common route is through skin contact, especially in individuals who have pre-existing skin lesions. Inhalation of paraquat is also a source of paraquat exposure. Usually, inhalation of spray is unlikely to cause systemic toxicity because of its low vapour pressure and the large droplets that are formed. However, when paraquat is used in a confined space, fatal pulmonary disease has occurred (paraquat spray in a green house [4]).

Paraquat toxicity can produce both local and systemic effects. The major acute local effects result from the caustic properties of the chemical. This includes ulceration of skin and cornea. In ingestion cases, the major effects are burning and ulceration of lips, tongue, pharynx and oesophagus, even to the point of producing a pseudomembrane reminiscent of diphtheria and oesophageal perforation. The acute systemic effects are mostly seen after massive ingestion(> 30 mg/kg or 50 mL of the paraquat concentrate). Patients may have pulmonary oedema, cardiac, renal, or hepatic failure, and convulsion. Death may occur within several hours to a few days caused by multiple organ failure.

The major subacute toxicity is the pulmonary effects, which is hallmark of paraquat poisoning. Pulmonary oedema begins 24 to 48 hours after ingestion and produces a syndrome resembling adult respiratory distress. It progresses to pulmonary fibrosis within a few days in a dose-dependent manner. The other subacute toxicity effects include renal failure, metabolic acidosis, myocarditis and necrosis of the adrenal glands.

Laboratory abnormalities include urine spot test for paraquat, sensitive only to 1 m g/ml. The use of radioimmunoassay has improved the delectability down to well below 0.1 m g/ml. RIA is useful for evaluating pulmonary function and renal function.

Goal of therapeutic management is primarily directed at removing paraquat from the gastrointestinal tract, increasing its excretion from blood and preventing pulmonary damages. To prevent GI absorption, gastric lavage should be performed using diatomaceous clays in the lavage solution. The lavage must be performed cautiously in view of the ulceration to prevent rupture or perforation. Activated charcoal and ion exchange resin also has been shown to be an effective absorbent. To remove paraquat from blood, the most effective ways are to maintain renal function in the early stages and to perform hemodialysis or hemoperfusion. The management of pulmonary damage is unique and important in paraquat poisoning. Lung changes in paraquat poisoning are similar to the direct toxicity of high alveolar oxygen tension. Thus, prevention of superoxide radical formation may be accomplished by using low 02 breathing mixtures. The low FIO_2 mixtures should be used to produce therapeutic hypoxemia. There are some reports showing that early administration of an antioxidant therapy, including deferoxamine and acetylcysteine, are useful to limit systemic toxicity [5]. The other methods to reduce oxygen toxicity have also been proposed such as cardiopulmonary bypass. Recently, there is some interest in using nitric oxide inhalation to treat paraquat-induced lung injury [6] Corticosteroids have traditionally been used as well as immunosuppressive agents, such as azathioprine and beclomethasone. D-propranolol can be used to displace paraquat from lung. Radiotherapy to prevent and treat pulmonary fibrosis is still controversial [7]. In severe paraquat-induced pulmonary fibrosis, lung transplantation has been performed, but without success [7, 8].

In summary, the paraquat poisoning throughout the world is not rare. The mortality is high. Recognising the clinical presentation and getting the exposure history, and early therapeutic management are critical to prevent irreversible pulmonary damage.

References

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